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Original Research

Assessment of left ventricular functions with myocardial performance index in coronary slow flow phenomenon

Evaluation of MPI in coronary slow flow phenomenon

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Abstract
Aim: Coronary slow flow phenomenon (CSFP) is the delayed filling and emptying of contrast agents in the coronary arteries without angiographically significant stenosis. The impact of CSFP on left ventricular (LV) functions is unclear. The myocardial performance index (MPI) is an index that permits the evaluation of LV systolic and diastolic functions together. In this study, we aimed to evaluate how LV systolic and diastolic functions are affected by the use of MPI in patients with CSFP.
Material and Methods: The study included 53 patients (28 men and 25 women) who were found to have CSFP on coronary angiography, and 53 age and gender-matched individuals (30 men and 23 women) with normal coronary arteries. Isovolumetric contraction time (IVCT), isovolumetric relaxation time (IVRT) and ejection time (ET) were measured for all participants included in the study with the help of the tissue Doppler technique. MPI values were calculated with the IVCT+IVRT/ET formula and the results were compared between groups.
Results: The mean age of the study group was 54.4 ± 9.9 years. In the CSFP group, the MPI was significantly higher (0.56 ± 0.09 vs 0.51 ± 0.09, p = 0.016), IVRT was longer (75.30 ± 11.83 vs 69.47 ± 15.89 ms, p = 0. 035), and ET was shorter (257.51 ± 30.98 vs 270.04 ± 21.4 ms, p = 0.017). IVCT was similar between groups (67.34 ±12.74 vs. 68.72 ± 13.42 ms, p = 0.588). LVEF, Mitral E and mitral A wave, E', A', and E/A were similar in both groups.
Discussion: Our study results demonstrated that conventional diastolic and systolic parameters were not affected in CSFP and MPI was impaired. We think that MPI should be measured together with other routine echocardiographic measurements when evaluating whether the left ventricular function is affected by CSFP.

Keywords
Coronary Slow Flow, Myocardial Performance Index, Left Ventricular Functions

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Introduction

Coronary slow coronary flow phenomenon (SCFP) is an entity characterized by a normal coronary artery on coronary angiography but slow antegrade progression of the contrast agent into the distal vascular structures [1]. Its incidence may vary between 1% and 7% [2]. Although the etiopathogenesis is not clear, underlying endothelial dysfunction, inflammatory process, increased vasoconstrictor response and decreased nitric oxide (NO) response have been associated with CSFP [3,4]. There are a limited number of studies in the literature on left ventricular functions (LV) in CSFP, but a myocardial performance index (MPI) assessment was not performed in these studies [5-7].

MPI is a useful predictive parameter that reflects the global performance of the myocardium, allowing joint assessment of systolic and diastolic functions of the heart [8,9]. It is not significantly affected by the geometric structure of the ventricle, preload, afterload, age and heart rhythm, and its important advantages are compared to other conventional diastolic parameters. Myocardial performance index (MPI), also known as the Tei index, is calculated by adding the isovolumetric contraction time (IVCT) and isovolumetric relaxation time (IVRT) and dividing it by the ejection time (ET) (MPI=IVCT+IVRT/ET) [10].

Our current study aims to compare left ventricular functions in patients with CSFP with a healthy control group using MPI. In this way, we think that we will evaluate both the systolic and diastolic functions of the left ventricle together.

Material and Methods

Study population

This study was designed as a single-center prospective and cross-sectional. We included 53 patients who underwent elective coronary angiography in our clinic between January 2021 and May 2022 and were diagnosed with CSFP. The control group consisted of 53 age and gender-matched participants with normal epicardial coronary arteries. All participants included in the study were informed about the study and written consent was obtained from those who accepted. A detailed physical examination was performed on the study population, and their medical history was questioned. Before the coronary angiography procedure, 12-lead surface ECGs were taken and analyzed. Those with normal sinus rhythm were included in the study to make the TDI assessment accurately. Institutional ethics committee approval was obtained from Seyh Edebali University for the study (Decision No: 2021/126170).

Those with known coronary artery disease, moderate to severe valve disease, severe left ventricular hypertrophy, severe arrhythmia, history of heart surgery, heart failure with reduced ejection fraction (LVEF ≤ 40%), and heart failure with mid-range ejection fraction (LVEF 41% – 49%), active infection period, the presence of pathological Q waves or left bundle branch block on the ECG, anemia (Hg <11 g/dL), thyroid dysfunction, pulmonary hypertension (sPAP >20 mm-Hg), ectasia appearance in coronary arteries, those of poor image quality were excluded from the study.

Echocardiographic evaluation

All participants underwent transthoracic echocardiographic evaluation after at least 5 minutes of rest. ECG electrodes were connected to monitor cardiac cycles. Measurements were made using the Philips brand EPIQ 7 device (Philips, Amsterdam, Netherlands) in the left lateral decubitus position as recommended by the American Society of Echocardiology. Aortic diameter, left atrium, LV end-diastolic and end-systolic diameters, right ventricular diameter and wall thickness were measured using the M-mode technique from the parasternal short long axis. Modified Simpson or Teichholz methods were used to calculate the left ventricular ejection fraction (LVEF). The presence of valvular dysfunction and pericardial fluid was also checked in the measurements.

During apical four-chamber imaging, transmitral flow samples were obtained from pulsed wave (PW) Doppler examination obtained by placing a sample volume at the tip of the mitral leaflets. PW Doppler examination of left ventricular filling, apical view Doppler sample volume was measured parallel to the long axis of the LV and at the level of the mitral annulus. Early diastolic mitral flow (E), late diastolic mitral flow (A) waves were measured by PW Doppler from the apical windows, and E/A ratios were calculated using these parameters. Early diastolic mitral annular (E'), late diastolic (A'), systolic peak velocities (S) were measured at the level of the annulus of the lateral edges of the left ventricle by tissue Doppler imaging (TDI). IVCT, IVRT and ET measurements were recorded and MPI was calculated with the formula (MPI = IVCT + IVRT / ET) (Figure 1). All measurements were recorded by a different cardiologist blinded to the patient data, with an average of 3 to 5 cardiac cycles.

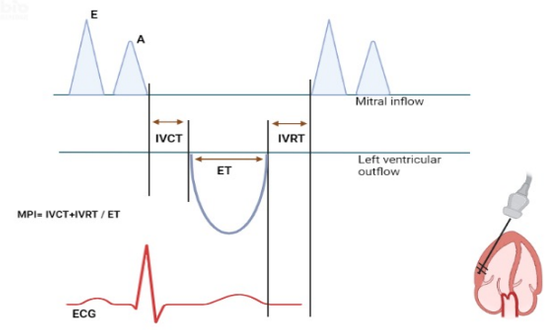

Figure 1. Myocardial performance index measurement by tissue Doppler imaging.

MPI: Myocardial performance index, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, ET: Ejection time, E: early diastolic mitral annular velocity, A: late diastolic velocity

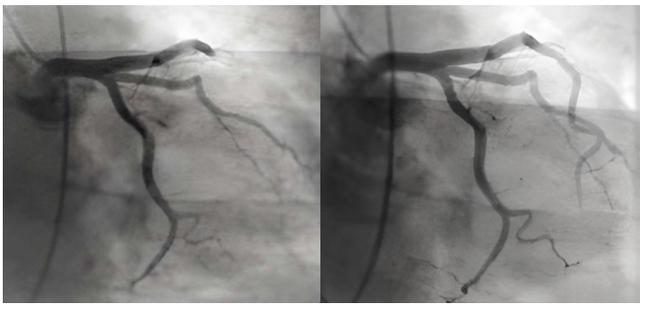

Figure 2. Coronary slow flow phenomenon in the LAD mid-region

Coronary angiography

Coronary angiography (CAG) was performed in the catheterization department of our hospital according to standard protocols. A digital imaging system (AXIOM Sensis; Siemens AG, Munich, Germany) was used for coronary angiographic imaging. All CAGs were independently evaluated by two different invasive cardiologists blinded to the clinical data of the study groups. Blood flow in the coronary vessel was assessed using thrombolysis in myocardial infarction frame count (TFC). The thrombolysis in myocardial infarction frame count (TFC) method was used for the quantitative measurement of coronary blood flow. As previously defined, the time taken for contrast agent to reach distal landmarks for each coronary artery was expressed as the number of frames. The starting point was taken as the moment when the contrast agent touched both sides of the artery and started to progress. As the final point, the moment when the contrast agent reaches the distal branching point called the mustache for the left anterior descending (LAD), the first lateral branch of the posterolateral artery for the right coronary artery (RCA), and the moment when the distal bifurcation of the longest branch is visualized for the circumflex (Cx) were taken. Since LAD has a longer course than the others, the corrected TFC (cTFC) was obtained by dividing the value found by 1.7. Patients with at least one coronary artery with a frame count above the given standard deviations of 20.4±3.0 for RCA, 22.2±4.1 for Cx, and 36.2±2.6 for LAD, were determined as coronary slow flow [11]. Coronary angiographic imaging of the slow flow phenomenon is shown in Figure 2.

Statistical analysis

Statistical Package for Social Sciences 21.0 for Windows (IBM SPSS Statistics for Windows, Armonk, USA) was used for data analysis. Continuous variables were tested for normal distribution with the Kolmogorov-Smirnov test. Numerical variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as percentages. Normally distributed continuous variables were compared with the "Student t-test" and non-normally distributed continuous variables were compared with the "Mann Whitney-U" test. The Chi-square test was used to compare categorical variables. A p-value of <0.05 was considered statistically significant.

Results

The mean age in the study group was 54.4 ± 9.9 years. There was no statistically significant age and gender difference between the groups. There is a statistically significant difference in the frequency of smoking between the two study groups (x2 = 5.386, p = 0.020). The frequency of smoking is greater in CSFP subjects. On the contrary, there is no significant difference in the frequency of hypertension (x2 = 0.168, p = 0.682), diabetes mellitus (x2 = 0.447, p = 0.504), hyperlipidemia (x2 = 0.043, p = 0.836) as well as family history (x2 = 0.229, p = 0.632) between CSFP and NCA subjects. Comparison of the clinical and demographic information of the patients is shown in Table 1.

In conventional echocardiographic measurements, aortic diameter, left ventricular end-diastolic diameter, right ventricular diameter, interventricular septum and posterior wall thickness were similar among groups. Conventional diastolic

Table 1. Demographic and clinical characteristics of the study population

	CSFP group (n=53) (Mean± SD)	NCA group (n=53) (Mean± SD)	p-value
Age (years)	54.15 ± 10.27	54.7 ± 9.68	0.778
Female gender	25 (47.2 %)	23 (43.4)	0.696
Hypertension, n (%)	19 (35.8 %)	17 (32.1%)	0.682
Diabetes mellitus, n (%)	15 (28.3 %)	12 (22.6 %)	0.504
Hyperlipidemia, n (%)	17 (32.1%)	18 (34%)	0.836
Smoking, n (%)	17 (32.1%)	7 (34%)	0.020
Family history, n (%)	12 (22.6 %)	10 (18.9%)	0.632
SBP, mm Hg	130.85 ± 13.28	128.96 ± 14.41	0.485
DBP, mm Hg	78.04 ± 11.14	78.26 ± 10.93	0.916

SBP Systolic blood pressure, DBP Diastolic blood pressure

Table 2. Comparison of echocardiographic parameters between groups

	CSFP group (n=53) (Mean± SD)	NCA group (n=53) (Mean± SD)	p-value
LVEF (%)	59.89 ± 3.61	59.28 ± 3.82	0.405
Aortic diameter (mm)	36.36 ± 3.49	36.68 ± 3.59	0.643
Left atrium (mm)	37.13 ± 4.01	36.13 ± 3.22	0.161
LVEDD (mm)	48.27 ± 3.77	47.53 ± 3.39	0.289
IVS (mm)	11 ± 1.33	10.64 ± 1.36	0.173
PW (mm)	10.75 ± 1.79	10.53 ± 1.47	0.483
E (cm/sec)	68.05 ± 13.89	71.37 ± 12.04	0.192
A (cm/sec)	77.03 ± 14.48	80.62 ± 11.43	0.160
E'	12.58 ± 2.72	13.54 ± 2.39	0.056
A'	10.88 ± 2.34	11.28 ± 2.34	0.386
S	10.26 ± 2.41	11.01 ± 2.17	0.094
E/A	0.90 ± 0.21	0.90 ± 0.20	0.984
E'/A'	1.20 ± 0.33	1.24 ± 0.29	0.481
IVCT (msn)	67.34 ±12.74	68.72 ± 13.42	0.588
IVRT (msn)	75.30 ± 11.83	69.47 ± 15.89	0.035
ET (msn)	257.51 ± 30.98	270.04 ± 21.4	0.017
MPI	0.56 ± 0.09	0.51 ± 0.09	0,016

CSFP: Coronary slow flow phenomenon, NCA: Normal coronary artery, LVEF: Left ventricular ejection fraction, LVEDD: Left ventricular end diastolic diameter, IVS: Interventricular septum, PW: Posterior wall, E: Early diastolic mitral inflow velocity, A: Late diastolic mitral inflow velocity, E': Early diastolic mitral annular velocity, A': Late diastolic mitral annular velocity, S: Peak systolic mitral annular velocity, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, ET: Ejection time, MPI: Myocardial performance index

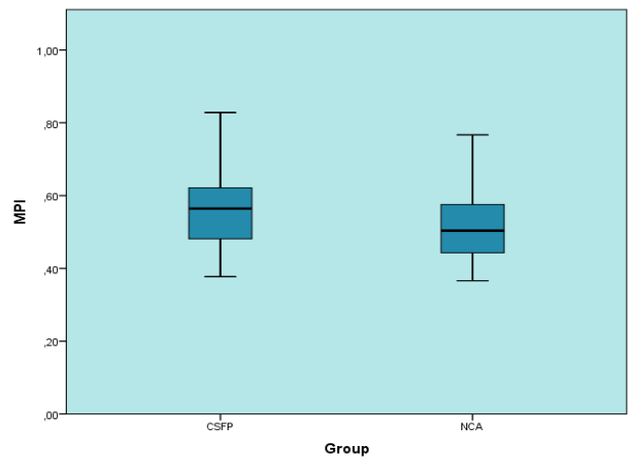

Figure 3. Comparison of MPI in CSFP and NCA groups.

function parameters were similar between the groups. In tissue Doppler measurements, while IVCT was similar between the CSFP and NCA groups (67.34 ±12.74 vs. 68.72 ± 13.42, p=0.588, respectively), the IVRT lengthened statistically in the patient group (75.30 ± 11.83 vs. 69.47 ± 15.89, p=0.035, respectively). ET was significantly shorter in the CSFP group compared to the controls (257.51 ± 30.98 and 270.04 ± 21.4, p=0.017, respectively). A statistically significant increase in MPI measurement was observed in the CSFP group compared to the control group (0.56 ± 0.09 vs. 0.51 ± 0.09, p = 0.016). Comparison of the echocardiographic features of the study groups is shown in Table 2. MPI comparison between groups is shown in Figure 3.

Discussion

The main finding of this study is the statistically significantly higher MPI in patients with CSFP on coronary angiography. Again, we found that IVRT used to calculate MPI was high in people with CSFP, and ET was low. These results ensure important evidence that left ventricular functions should be monitored and precautions should be taken in the early period in individuals with CSFP. Our study is also the first in the literature to report an increase in MPI in those with CSFP.

CSFP is a rare entity in coronary angiography. Although its etiopathogenesis is not fully understood, it has been suggested in previous studies that different pathophysiological mechanisms such as endothelial dysfunction, microvascular disease, atherosclerosis, insufficient NO synthesis, and increased vasoconstrictor response may be involved in the molecular basis of CSFP [12-14]. However, previous studies have demonstrated the long-term prognostic significance of CSFP in the development of future major adverse cardiovascular events [15,16]. It has been reported in many studies that it increases the risk of thrombosis, predisposes to the development of atherosclerosis, and causes recurrent angina attacks and ventricular arrhythmias [17-19]. Therefore, CSFP should not be considered a completely benign condition. Another unknown is the long-term effects on cardiac functions. There are studies in the literature showing that systolic and diastolic functions of the left ventricle may be impaired in patients with CSFP. A recent echocardiographic study reported impaired global longitudinal strain (GLS) in patients with CSFP [6]. Similarly, Wang Y et al. reported the deterioration of right and left ventricular functions in CSFP patients using the two-dimensional speckle-tracking echocardiography method [20]. The difference in both studies from ours was that MPI and its constituent parameters were not used in the studies. As it is known, GLS evaluation is not an examination that can be performed in every clinic, and its application requires experience. However, MPI measurement is a repeatable and cheaper method that can be easily measured in TDI. In addition to these advantages, the fact that it is not affected by heart rate, afterload, and preload may make MPI a more reliable parameter in the evaluation of ventricular functions. In the study by Zhu X et al. on 45 CSFP patients, right ventricular functions were evaluated and a significant increase in right ventricular MPI was observed [21]. In our study, however, LV functions were evaluated and it was observed that LV MPI increased significantly. In addition, in our study, we showed that the parameters that make up MPI, IVRT lengthened and ET shortened. IVRT is a high-energy dependent very active phase. If sufficient adenosine triphosphate (ATP) cannot be produced in the myocardium due to ischemia, lactic acid accumulates, which prolongs the separation time of the contractile elements. This is not unique to ischemia, but also occurs in LV dysfunction and indirectly causes ischemia.

The study by Javadi DH et al. differed from other studies in terms of results. Using conventional echocardiographic methods in their study, they reported that systolic and diastolic parameters were not affected in CSFP patients [22]. Conventional echocardiographic parameters were not affected in our study either. The part of our study that we thought was superior was the assessment of ventricular functions with a more sensitive scale, the MPI. In addition, the number of patients was relatively higher than in this study. Conventional echocardiography may not be an adequate method to screen for some dysfunctions in patients with CSFP, and other echocardiographic methods such as TDI may be considered. TDI has been shown to have an excellent ability to measure regional myocardial dysfunction and better performance in patients with CSFP [23]. Based on all this evidence, we can say that IVCT, IVRT, ET and MPI can also be used in routine follow-up in CSFP considering the effectiveness of evaluating ventricular functions. As a matter of fact, in many previous studies, it has been reported that MPI and its parameters can be used in the follow-up of many diseases that can cause ventricular dysfunction [24,25].

Conclusion

Our study showed that MPI, which allows assessment of both systolic and diastolic functions of the ventricles, is prolonged in CSFP patients. In addition, we found that the IVRT used to calculate the MPI lengthened and the ET shortened. In our opinion, MPI can be readily measurable by echocardiography and can inform that can help guide the management of CSFP patients.

Limitations

One of the main limitations of the study is that the data were obtained from a single center. Since it was designed as an echocardiographic study, it does not show conclusions about the molecular mechanisms that cause ventricular dysfunction of CSFP. Another limitation of our study is the relatively small number of patients. We think that our study should be repeated in multiple centers and on a large population to support our results.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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